REMARKS

Claims 1-4 have been amended to better claim the invention by reciting α7A integrin and muscle tissue samples. These amendments are supported by the as-filed Specification at page 6, lines 34-36 and at page 1, lines 25-27. Claims 7-23 are canceled without prejudice. Entry of new claim 24 is respectfully requested; support for this claim is found in the as-filed Specification at page 28, for example. None of the amendments made herein constitutes the addition of new matter.

The Requirement for Restriction

The Patent Office has made the requirement for restriction under 35 U.S.C. 121 final, alleging that the claims as filed embody six separately patentable inventions; Groups I and II are set forth below.

I. Claims 1-3, drawn to a method of identifying an individual exhibiting symptoms of a muscular dystrophy comprising obtaining a tissue sample from the individual which is known in a normal individual to express α7β1 and determine the level of the translation of the α7β1 integrin using an antibody, classified in Class 435, subclass 7.1.

II. Claims 1 and 4-6, drawn to a method of identifying an individual exhibiting symptoms of a muscular dystrophy comprising obtaining a tissue sample from the individual which is known in a normal individual to express α7β1 using reverse transcriptase-polymerase chain reaction, classified in Class 435, subclass 6.

Applicants have elected (with traverse) the claims of Group I, claims 1-3, drawn to a method of identifying an individual exhibiting systems of a muscular dystrophy using antibody.

Applicants again respectfully request the rejoinder of the claims of Group II, claims 1 and 4-6, drawn to a method of identifying an individual exhibiting systems of muscular dystrophy using reverse transcriptase polymerase chain reaction. Applicants note that the same type of muscular dystrophy, namely scapuloperoneal muscular dystrophy, is identified by both methods, and the method measures expression of the same gene, α7A integrin, in the two methods. The difference is the particular details of the methods, i.e. the use of antibody or the use of nucleic acid primers in a RT-PCR assay.

Because claim 1 is a linking claim which links the Group I (antibody) and the Group II (PCR) claims and because of the common technical feature of measuring α7A integrin expression, Applicants again respectfully request the claims 1-6 be examined together. Applicants respectfully submit that a search of both groups would not constitute an undue burden on the Patent Office, given the common technical feature.

The Objections

Claim 3 has been objected to based on a typographical error. Applicants have correctly presented this claim in the present Amendment. The claim was correct as filed, although there was an inadvertent error in the prior submission.

The Rejections under 35 U.S.C. 112, second paragraph

Claims 1-3 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite.

Claim 1 is allegedly indefinite for being incomplete for omitting essential elements, such omission amounting to a gap for the detection step. The Examiner has indicated that the omitted element is the antibody that specifically binds the integrin to detect the translation product.

Applicants have amended claim 1 to rectify the omission by reciting the use of a detectable α7A-specific antibody, and withdrawal of the rejection is requested.

The Rejections under 35 U.S.C. 112, first paragraph

Claim 1 has been rejected under 35 U.S.C. 112, first paragraph, as allegedly not enabled. Applicant respectfully traverses this rejection.

The Patent Office has alleged that the Specification does not provide enablement for a method for identifying an individual exhibiting symptoms of a dystrophy as having scapuloperoneal muscular dystrophy by analyzing any tissue. The Patent Office has also alleged that the Specification teaches no way other than the use of an α integrin specific antibody to monitor the translation product in the tissue sample

In the interest of advancing prosecution and without acquiescing to the rejection, Applicant has amended claim 1 to specify that a muscle tissue sample and to specify that an α7A integrin specific antibody is used. These amendments are supported by the as-filed Specification at page 6, lines 34-36, and at page 7, lines 9-32, and in Examples 4-7.

In view of the amendments to the claims and the well known high level of skill in the relevant art, Applicant respectfully requests the withdrawal of the rejection under 35 U.S.C. 112, first paragraph.

The Rejections under 35 U.S.C. 102(b)

Claims 1-3 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Hayashi et al. (1998). Applicant respectfully traverses this rejection.

The Hayashi reference is alleged to teach a method for identifying an individual exhibiting symptoms of muscular dystrophy. Antibodies against the extracellular domain of integrin α7, integrin β1D, α2 laminin and dystrophin were used with muscle biopsies from patient with unclassified congenital myopathy and congenital muscular dystrophy. Hayashi was said to further disclose determination of the level of the α7 integrin in skeletal muscle samples from control and three patients with primary integrin α7 deficiency. Hayashi is said to teach that those three patients showed normal laminin expression, dystrophy can and sarcoglycan.

The Examiner has acknowledged that the reference is silent on scapuloperoneal muscular dystrophy but that the patients had the same symptoms as SPMD. Claim 1 has been amended to specify that the patients tested exhibit symptoms affecting the muscles of the shoulder girdle and peroneal. Applicant respectfully notes that there is no disclosure of these particular symptoms exhibited by the three integrin-negative, laminin positive patients tested by Hayashi et al. Moreover, those three patients tested by Hayashi et al. were 8 months, 4 years and 11 years of age. The present Specification, at page 1, teaches that scapuloperoneal muscular dystrophy "has late onset, with affected individuals first displaying symptoms in their late teens or early twenties and up to the late fifties." Therefore it is most unlikely that the infant and children tested by Hayashi et al. suffered from scapuloperoneal muscular dystrophy, as described in the present application, which is also characterized as late onset muscular dystrophy.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicant has amended to include the step of diagnosing and to recite the symptoms of the patient in whom diagnosis is sought.

In view of the amendments to claim 1 and the discussion provided herein, Applicant respectfully maintains that the present invention is not anticipated by the cited Hayashi et al. reference, and the rejection must be withdrawn.

The Rejections under 35 U.S.C. 103

Claims 1-3 have been rejected under 35 U.S.C. 103(a) as allegedly obvious over Hayashi et al. as evidenced by the Specification at page 22, lines 7-13 in view of Hodges et al. (1997). Applicant respectfully traverses this rejection.

The Hayashi reference was discussed in the context of the Section 102 rejection. The Patent Office has characterized the claimed invention as differing from the reference teachings only by the recitation of an $\alpha 7\beta 1$ integrin-specific antibody in claim 2 wherein the $\alpha 7\beta 1$ integrin-specific antibody is detectably labeled in claim 3.

Hodges is said to teach that the antiserum 347 reacts with native and denatured $\alpha 7\beta 1$ integrin and binding is inhibited by prior reaction with the immunizing peptide. Further Hodges et al. is said to teach that the $\alpha 7\beta 1$ integrin is the primary laminin receptor on skeletal muscle myoblasts and adult myofibers. Hodges et al. also teaches that immunofluorescent (assays) demonstrates an increase in $\alpha 7\beta 1$ integrin in patients with Duchenne muscular dystrophy and *mdx* mice that lack dystrophin.

The Patent Office has concluded that it would have been obvious at the time the invention was made to substitute the $\alpha 7$ antibody taught by the Hayashi reference with the 347 antibodies that react with native and denatured integrin in a method for identifying an individual exhibiting symptoms of muscular dystrophy as well as an individual suffering from scapuloperoneal muscular

dystrophy. The Patent Office has further alleged that one of ordinary skill in the art would have had a reasonable probability of success in producing the claimed invention.

Applicant notes the amendments to claim 1 which specifies particular symptoms of the patients to be tested and that the antibody (or transcription product assay) is specific for α7A integrin. Applicant has discussed the Hayashi et al. reference above; the patients therein included an infant and two children; the present application (page 1) teaches that those afflicted with scapuloperoneal muscular dystrophy present symptoms relatively late in life – late teens to the fifties. In addition, although the Hayashi reference teaches that there were three patients who expressed laminin but not α integrin, there was no diagnosis of scapuloperoneal muscular dystrophy as a result of that characterization.

The Hodges reference teaches the complexity of the proper association of muscle fibers with nerves and cell membranes. The experiments described by the Hodges reference were designed to characterize the protein patterns of Duchenne and Becker muscular dystrophy patients. There is no mention of patients suffering from scapuloperoneal muscular dystrophy, let alone any guidance as to the particular pattern of protein expression in those patients.

Applicant respectfully maintains that the combined teachings of the Hayashi and Hodges references do not lead one to the present invention, as claimed. At most these references might invite one to carry out experiments to determine the protein expression patterns associated with particular forms of muscular dystrophies, but there is nothing which would allow one to predict what those patterns would be. An invitation to experiment is not the proper basis for a proper, *prima facie* rejection for obviousness.

The courts have cautioned the Patent Office against a hindsight reconstruction of the invention. The suggestion must come from the cited references, not from information taken from an applicant's disclosure. The courts have cautioned the Patent Office against the impermissible use of hindsight. See, e.g., In re Dow Chemical Co., 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988) ("The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art . . . Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure.") Smithkline Diagnostics, Inc. v. Helena Laboratories Corp., 8 U.S.P.Q.2d 1468, 1475 (Fed. Cir. 1988). The Patent Office "cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention." Smithkline Diagnostics, Inc. v. Helena Laboratories Corp., 8 U.S.P.Q.2d 1468, 1475 (Fed. Cir. 1988).

In the interest of advancing prosecution and without acquiescing to the rejection, claim 1 has been amended to recite the particular symptomology of the patient being diagnosed, and a step of diagnosing has also been added.

In view of the foregoing, Applicant respectfully maintains that no *prima facie* case for obviousness has been made, and the rejection must withdrawn.

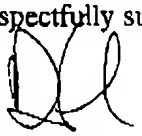
Conclusion

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This response is accompanied by a Petition for Extension of Time (one month) and authorization to charge the necessary fee. It is believed that the present Amendment does not require any petition for extension of time or the payment of any fees pursuant to 37 C.F.R. 1.16-1.17. If the this is incorrect, however, please grant any additional extension of time and deduct from Deposit Account No. 07-1969 the amount due under the foregoing Rules.

Respectfully submitted,



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